



Adenine nucleotide translocase 2 is a key mitochondrial protein in cancer metabolism

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Résumé en anglais	Adenine nucleotide translocase (ANT), a mitochondrial protein that facilitates the exchange of ADP and ATP across the mitochondrial inner membrane, plays an essential role in cellular energy metabolism. Human ANT presents four isoforms (ANT1-4), each with a specific expression depending on the nature of the tissue, cell type, developmental stage and status of cell proliferation. Thus, ANT1 is specific to muscle and brain tissues; ANT2 occurs mainly in proliferative, undifferentiated cells; ANT3 is ubiquitous; and ANT4 is found in germ cells. ANT1 and ANT3 export the ATP produced by oxidative phosphorylation (OxPhos) from the mitochondria into the cytosol while importing ADP. In contrast, the expression of ANT2, which is linked to the rate of glycolytic metabolism, is an important indicator of carcinogenesis. In fact, cancers are characterized by major metabolic changes that switch cells from the normally dual oxidative and glycolytic metabolisms to an almost exclusively glycolytic metabolism. When OxPhos activity is impaired, ANT2 imports glycolytically produced ATP into the mitochondria. In the mitochondrial matrix, the F1F0-ATPase complex hydrolyzes the ATP, pumping out a proton into the intermembrane space. The reverse operations of ANT2 and F1F0-ATPase under glycolytic conditions contribute to maintaining the mitochondrial membrane potential, ensuring cell survival and proliferation. Unlike the ANT1 and ANT3 isoforms, ANT2 is not pro-apoptotic and may therefore contribute to carcinogenesis. Since the expression of ANT2 is closely linked to the mitochondrial bioenergetics of tumors, it should be taken into account for individualizing cancer treatments and for the development of anticancer strategies.
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Liens

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